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Tailoring therapy to improve the treatment of children with obstructive sleep apnea according to grade of adenotonsillar hypertrophy

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ABSTRACT

Background: Obstructive sleep apnea (OSA) is a common disease in children with the major causes of hypertrophy of adenoid or tonsil and nasal diseases. The treatment methods for this disease include the resection of adenoid or tonsil, and drug therapy as well. However, no agreement on the selection of treatment method is available to date.

Objective: To investigate the individualized treatment methods for children with OSA with different sizes of adenoids and tonsils.

Methods: Children with OSA (diagnosed by polysomnography) were included into groups A (adenoid/tonsil grade ≤III) and B (adenoid/tonsil grade = IV), and further subdivided into subgroups A1 (3-month medication), A2 (3-month medication and negative-pressure sputum aspiration [NPSA]), B1 (3-month medication plus NPSA), B2 (coblation adenotonsillectomy with preoperative/postoperative medication for 3 days/2 weeks) and B3 (coblation adenotonsillectomy with preoperative/postoperative medication for 2 weeks/3 months). Six-month outcomes included quality of life for children with obstructive sleep apnea-18 item (OSA-18), obstructive apnea index (OAI), apnea hypopnea index (AHI) and lowest oxygen saturation ($LSaO_2$).

Results: Three hundred and eighty six patients (310 male; 6.70 ± 2.44 years-old) were included. Preoperative OSA-18, OAI, AHI and $LSaO_2$ were not significantly different. At all postoperative time points, subgroup A2 had significantly lower OSA-18 than subgroup A1; postoperative improvements in OAI, AHI and $LSaO_2$ were also superior in subgroup A2 ($P < 0.05$). The initial decrease in OSA-18 was not maintained in subgroups B1 and B2, whereas subgroup B3 showed a sustained reduction at 6 months. OAI and AHI were more improved in subgroup B3 ($P < 0.05$). Surgical/anesthetic complications in subgroups B2 and B3 were 5.5% and 0%.

Conclusion: Conservative therapy could achieve satisfactory outcomes in children with grade III hypertrophy, while surgery and drugs could achieve good outcomes in grade IV.

1. Introduction

Obstructive sleep apnea (OSA) also known as obstructive sleep apnea hypopnea syndrome is a common pediatric disease (prevalence of 1–3%) most commonly caused by adenotonsillar hypertrophy [1–3]. OSA is characterized by reduced oro-nasal airflow and oxygen desaturation, and is clinically manifested by snoring, mouth breathing, periods of apnea, restless sleep, urinary incontinence, inattentiveness, daytime hyperactivity, mood swings and failure to thrive [3]. Since OSA is associated with neurobehavioral deficits and serious complications (including growth retardation, cardiac dysfunction, conductive deafness and craniofacial malformations [4,5]), timely diagnosis and treatment are important [6–8].

Adenoidectomy and tonsillectomy are the primary treatments for OSA [8–12], although symptoms in some children improve little or even recur [13]. Continuous positive airway pressure (CPAP) is an option [14], but it is reported that patients have a low compliance to this therapy [15]. Although drug therapy is beneficial [16], surgical intervention is still required in some patients. Despite the various options available, the management of children with OSA still lacks an international set of standardized criteria.

Previous studies showed that adenoidal hypertrophy, tonsillar hypertrophy, sinusitis and inflammatory strictures in the nasal

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cavity are important risk factors for OSA in children [4,17]. Tonsil and adenoid sizes are positively related to OSA risk and severity [18,19]. Tonsils and adenoids of grades III and IV can obstruct the airways and be a primary cause of OSA [4]. Therefore, tonsil and adenoid size should be considered when selecting treatment options. Additionally, hypopnea and apnea occur repeatedly in children with OSA, especially in those with moderate or severe disease. This often produces a hypoxic and hypercapnic state that causes dysfunction of vital organs, including the heart, lung, liver and kidney [4,20], and reduces the sensitivity of the respiratory center to elevated carbon dioxide concentrations, maintaining the central respiratory center excitability by stimuli from carotid and aortic body chemoreceptors. In this situation, removal of the upper airway obstruction by surgery can cause a sudden rise in oxygen partial pressure and respiratory depression [21–23], increasing the surgical and anesthetic risks. Adequate preoperative preparation can reduce these risks. Therefore, it is important to adopt an individualized and tailored therapeutic approach for children with OSA, based on the tonsil and adenoid grades and disease severity.

The aims of the present study were to retrospectively assess pediatric patients with OSA seen at our otolaryngology department over a 3-year period, and to explore the efficacy of individualized treatments tailored to the grade of their hypertrophy.

2. Materials and methods

2.1. Patients

This was a retrospective study of pediatric patients diagnosed with OSA and treated at the Department of Otolaryngology, Children's Hospital of Fuzhou (Fujian Province, China) between June 2008 and April 2011. The study was approved by the Ethics Committee of the Children's Hospital of Fuzhou. Individual consent was waived by the committee.

Inclusion criteria were: (1) patient aged 1–13 years, pre-pubescent, and had consistent living conditions; (2) patient had been monitored by polysomnography (PSG) and complied with relevant criteria [4]; (3) patient had been examined using a tongue depressor or video laryngoscopy, and assessed for body weight (obesity) and total IgE; (4) OSA was considered to be caused by rhinosinusitis, adenoid hypertrophy and/or tonsillar hypertrophy; and (5) patient had been screened using the obstructive sleep apnea-18-item (OSA-18) questionnaire [24,25], administered by a specialist. Children who had unbalanced grade of tonsillar and adenoidal hypertrophy (one was grade III and the other grade IV) were excluded because they could not be classified into one of the groups for the study. Children with serious anatomic abnormalities of the mouth, nose or pharynx, or a history of massive trauma or any other chronic disease affecting the heart, lung, liver, kidney or brain were also excluded.

2.2. Diagnosis of OSA

OSA was diagnosed by sleep monitoring using the Alice 5 Sleep Diagnostic System (Philips Healthcare, Best, The Netherlands), Alice PDx Portable Sleep Diagnostic System (Philips Healthcare) and Jaeger PSG (Jaeger Ausbau GMBH & Co Kg, Würzburg, Germany), according to published criteria [26]. The time of obstructive apnea index (OAI) >1/h or the apnea hypopnea index (AHI) >5/h in every night's sleep was considered as abnormal; hypopnea was defined as the peak signal of the oral and nasal air current decreased by 50% and the oxygen saturation decreased by >0.03 and/or wake up. The duration of respiratory events was defined as ≥2 respiratory cycles [26].

Tonsillar hypertrophy was diagnosed by visual inspection, using a tongue depressor: tonsil size was graded I to IV; a tonsil size of grade III or IV with the presence of clinical symptoms was considered as tonsillar hypertrophy [27]. Adenoidal hypertrophy was diagnosed using a Pentax VNL-1530T video laryngoscope (Pentax, Tokyo, Japan): adenoid size was graded I to IV; an adenoid size of grade III or IV with the presence of clinical symptoms was considered as adenoidal hypertrophy [28]. The diagnosis of rhinitis and rhinosinusitis were made on the basis of published criteria [29,30].

2.3. Grouping and therapy

2.3.1. Grouping

Patients were included into two groups according to their original diagnosis: group A, adenoid and tonsil grade ≤III; and group B, adenoid and tonsil grade IV. Then, according to the original treatment that was undertaken, Group A was further subdivided into subgroups A1 (drug therapy for 3 months) and A2 (drug therapy plus negative-pressure sputum aspiration [NPSA] for 3 months). Group B was subdivided into subgroups according to original treatments: B1 (drug therapy plus NPSA for 3 months), B2 (coblation adenotonsillectomy after 3 days of drug therapy, followed by postoperative drug therapy for 2 weeks) and B3 (coblation adenotonsillectomy after 2 weeks of drug therapy, followed by postoperative drug therapy for 3 months). In our clinical practice, children ≤3 years old with adenoid and tonsil grade IV according to Chinese guidelines are considered a high risk population for surgery, and do not undergo surgery; therefore, they were all included in group B1, alongside other children whose parents or guardians had decided against surgery [4,29].

2.3.2. Therapy

Local drug therapy, administered for 3 months, consisted of nasal inhalation of 1 mL budesonide suspension in children <3 years old [31], and mometasone furoate nasal spray in children ≥3 years old [32,33]. Systemic drug therapies included oral antibiotics (for 2 weeks), Sinupret drops (for 4 weeks; a mixture of herbal products; elder (*Sambucus nigra*, Caprifoliaceae) flowers, primrose (*Primula veris*, Primulaceae) flowers with calyx, common sorrel (*Rumex acetosa*, Polygonaceae) herb, European vervain (*Verbena officinalis*, Verbenaceae) herb, and gentian (*Gentiana lutea*, Gentianaceae) root) and montelukast sodium (for 3 months) [34]. The drug dosages were as recommended by the manufacturers.

NPSA was given as an assisted therapy prior to budesonide or mometasone. Aspiration frequency was adjusted to between 1/day to 2/week. For aspiration, the patient was reclined in the supine position with the head tilted backwards. Three drops of 0.5% ephedrine were instilled into both nostrils. After nasal mucosal engorgement had subsided and a no. 6 suction tube was inserted into the nasopharynx via the nasal cavity, secretions were aspirated (aspirator pressure, 200 mmHg), alternating between nasal cavities.

Surgical therapies included adenotonsillectomy under a low-temperature plasma system. General anesthesia was achieved via endotracheal intubation. The whole tonsil was resected from its lower pole along the capsule, using an Evac 70 radio-frequency knife (Arthrocare Corporation, Austin, TX, USA). The adenoid was endoscopically resected layer by layer from the posterior wall to the ceiling of the nasopharynx, until the bilateral choanae and tori were fully exposed.

2.4. Follow-up and evaluation indexes

Efficacy was assessed using the obstructive apnea index (OAI), apnea hypopnea index (AHI) and the lowest oxygen saturation ($LSaO_2$) [4] measured by PSG before and 3 months after treatment. OSA-18 [24,25] was assessed before treatment, and at 1 week, 2 weeks, 1 month, 2 months, 3 months and 6 months after treatment. OSA-18 scores ranged from 18 to 126 points, 18–36 being regarded as normal, 37–59 as mild, 60–80 as moderate, and 81–126 as

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Table 1
Characteristics of the patients ($n = 386$).

Characteristics	Values
Gender (n) (%)	
Male	310 (80.3)
Female	76 (19.7)
Disease course, range	2 Weeks to >10 years
Repeated waking (n) (%)	56 (14.5)
Hyperhidrosis (n) (%)	101 (26.2)
Daytime sleepiness (n) (%)	13 (3.4)
Changes in behavior (n) (%)	14 (3.6)
Inattention, memory loss, poor academic performances (n) (%)	35 (9.1)
Growth retardation (n) (%)	85 (22.0)
Craniofacial characteristics (n) (%)	41 (10.6)
Lower respiratory tract infections (n) (%)	9 (2.3)
Cardiopulmonary and/or renal dysfunction (n) (%)	32 (8.3)
Nasal irritation and/or sneezing (n) (%)	206 (53.4)
Upper respiratory tract infections (n) (%)	358 (92.7)

severe [21,22]. Additionally, in subgroup B3, $LSaO_2$ and lesions in the heart, lung, liver and kidney were assessed before and 2 weeks after therapy using physical examination, blood tests (transaminases, blood urea nitrogen and creatinine) and X-rays. Complications associated with intraoperative anesthesia were compared between subgroups B2 and B3. Decreases in secretions were subjectively assessed using video laryngoscopy.

2.5. Statistical analysis

Statistical analysis was performed using SPSS 17.0 (SPSS Inc., Chicago, IL, USA). Data normality was assessed using the Kolmogorov–Smimov test. Quantitative data are expressed as means ± standard deviations (SDs), and categorical data as frequencies. Comparisons between groups were made using repeated measurement analysis of variance, paired t-tests, χ^2 tests or Fisher's exact tests, as appropriate. $P < 0.05$ was considered statistically significant.

3. Results

3.1. Patient characteristics

Three hundred and eighty six patients (310 male) were included, with a mean age of 6.70 ± 2.44 years (range: 1–13 years). All patients had a diagnosis of OSASH by PSG. Details of disease course duration, and symptoms experienced by all patients are presented in Table 1.

Ninety patients (23.3%) were included in group A, with 44 (11.4%) in subgroup A1 and 46 (11.9%) in subgroup A2; and 296 (76.7%) into group B, with 68 (17.6%) in subgroup B1, 109 (28.2%) in subgroup B2 and 119 (30.8%) in subgroup B3. Table 2 shows the patient characteristics before any treatment; there were no significant differences between any of the groups in gender, age, BMI, PSG-monitored variables (OAI, AHI and $LSaO_2$) or OSA-18 score.

3.2. Comparison of OSA-18 scores between subgroups A1 and A2

Fig. 1 shows pre-treatment and post-treatment OSA-18 scores in subgroups A1 and A2. Progressive post-treatment reductions in OSA-18 scores were observed in both subgroups (although subgroup A1 showed a small increase in OSA-18 score from 3 to 6 months). There was no significant difference in the pre-treatment OSA-18 value between subgroups A1 and A2. However, for all post-treatment time points, the OSA-18 value was significantly lower in subgroup A2 than in subgroup A1 ($P < 0.05$).

3.3. Comparison of PSG indexes between subgroups A1 and A2

Table 3 presents pre-treatment and post-treatment OAI, AHI and $LSaO_2$ in subgroups A1 and A2. In both subgroups, treatment was associated with significant reductions in OAI and AHI, and significant increases in $LSaO_2$ (all $P < 0.05$). Furthermore, the improvements in all three indexes were significantly more important in subgroup A2 compared with subgroup A1 ($P < 0.05$).

3.4. Comparison of OSA-18 scores between subgroups B1–B3

Fig. 2 shows pre-treatment and post-treatment OSA-18 scores in subgroups B1–B3. There were no significant differences between the three subgroups in pre-treatment OSA-18 values. OSA-18 scores in subgroups B1 and B3 decreased progressively up to 3 months post-treatment, before stabilizing (subgroup B3) or increasing slightly (subgroup B1). In subgroup B2, the OSA-18 score decreased up to 1 month after treatment, before showing a progressive small increase up to 6 months. Although subgroup B2 showed the most important post-treatment reduction during the first 2 weeks, the lowest OSA-18 score at 6 months was in subgroup B3, with subgroup B1 showing the highest score at 6 months. OSA-18 scores differed significantly between the B1–B3 subgroups at every time point, except for B1 vs. B3 at 2 weeks.

3.5. Comparison of PSG indexes between subgroups B1–B3

Table 4 shows pre-treatment and post-treatment OAI, AHI and $LSaO_2$ in subgroups B1–B3. In all three subgroups, therapy

Table 2
Baseline characteristics of the patients according to adenoid and tonsil grade.

		Adenoid and tonsil ≤ grade III		*P*-value	Adenoid and/or tonsil ≤ grade IV			*P*-value
		Subgroup A1 (44)	Subgroup A2 (46)		Subgroup B1 (68)	Subgroup B2 (109)	SubgroupB3 (119)	
Gender (cases) Male:female		39:5	36:10	0.187	51:17	82:27	102:17	0.088
Age (years)		6.89 ± 2.61	6.89 ± 2.64	0.993	6.57 ± 2.13	6.80 ± 2.50	6.55 ± 2.44	0.708
BMI (kg/m^2)		16.47 ± 2.24	16.31 ± 1.92	0.710	16.60 ± 2.25	16.54 ± 2.42	16.44 ± 2.31	0.901
Indices monitored by PSG	OAI (times/h)	3.51 ± 2.80	4.42 ± 3.08	0.145	4.83 ± 2.99	5.32 ± 8.49	4.54 ± 5.52	0.658
	AHI (times/h)	7.85 ± 6.47	10.54 ± 20.49	0.407	11.82 ± 16.21	16.30 ± 22.55	13.72 ± 15.11	0.269
	$LSaO_2$ (%)	86.98 ± 5.06	85.72 ± 6.66	0.316	83.75 ± 3.15	83.65 ± 8.71	83.98 ± 7.72	0.944
OSA-18 score		73.68 ± 13.15	72.78 ± 14.09	0.755	73.97 ± 18.22	73.28 ± 15.77	75.61 ± 16.33	0.554

Note: AHI, apnea hypopnea index; BMI, body mass index; $LSaO_2$, the lowest recorded arterial oxygen saturation; OAI, obstructive apnea index; PSG, polysomnography.

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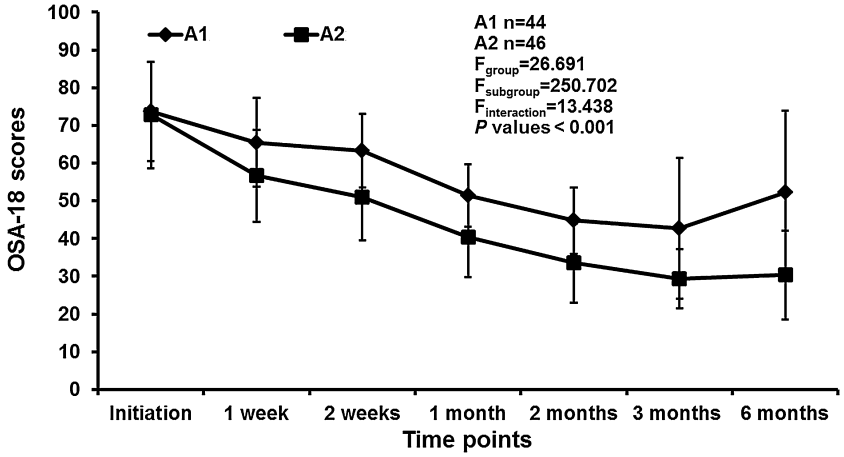

Fig. 1. OSA-18 scores of patients in the A1 and A2 subgroups before and after treatment. Results are presented as mean ± standard deviation. $P < 0.001$ initiation vs. 6 months.

Table 3
Comparison of the PSG-monitored indices between the A1 and A2 subgroups.

Group (cases)	OAI (times/h)		AHI (times/h)		$LSaO_2$ (%)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
A1 subgroup (44)	3.51 ± 2.80	1.05 ± 0.91	7.85 ± 6.47	5.63 ± 2.97	86.98 ± 5.06	92.57 ± 2.76
A2 subgroup (46)	4.42 ± 3.08	0.47 ± 0.38	10.54 ± 20.49	2.28 ± 2.22	85.72 ± 6.66	93.96 ± 2.08
Between-group effect	$P < 0.05$		$P < 0.05$		$P < 0.05$	
Inter-group effect in A1 subgroup	$P < 0.001$		$P < 0.001$		$P < 0.001$	
Inter-group effect in A2 subgroup	$P < 0.001$		$P < 0.001$		$P < 0.001$	

Note: AHI, apnea hypopnea index; $LSaO_2$, the lowest recorded arterial oxygen saturation; OAI, obstructive apnea index; PSG, polysomnography.

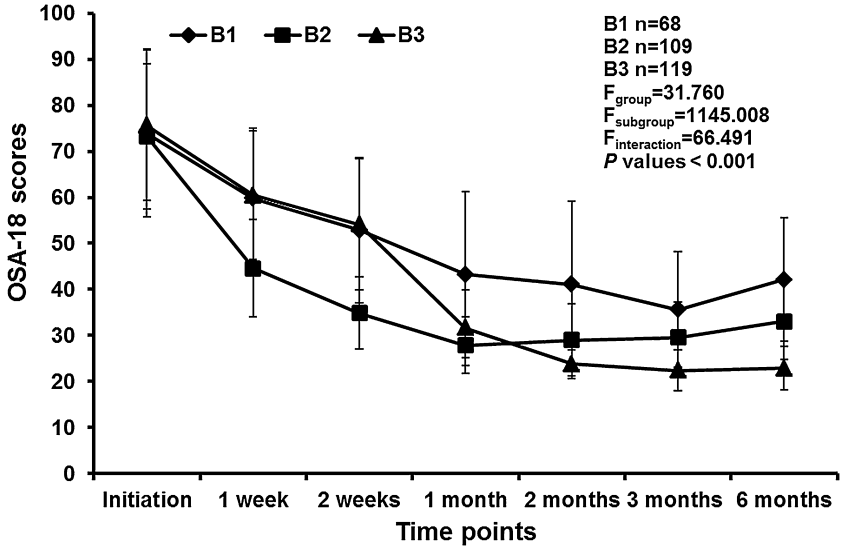

Fig. 2. OSA-18 scores of patients in the B1–B3 subgroups before and after treatment. Results are presented as mean ± standard deviation. $P < 0.001$ initiation vs. 6 months.

was associated with significant decreases in OAI and AHI, and significant increases in $LSaO_2$ ($P < 0.05$). Inter-group analysis indicated that the improvements in OAI and AHI were more important in subgroup B3 and smaller in subgroup B1 ($P < 0.05$). In addition, post-treatment $LSaO_2$ was significantly lower in subgroup B1 than in the other subgroups ($P < 0.05$), with no significant difference between subgroups B2 and B3.

3.6. Efficacy analysis of adjuvant therapy plus 2-week preoperative drug therapy for patients in subgroup B3 with moderate/severe scores

Patients in subgroup B3 with moderate or severe scores, treated by adjuvant therapy and a 2-week preoperative drug therapy, showed significantly reduced secretions in the nasal cavity and nasopharynx. After treatment, there were marked improvements

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Table 4
Comparison of indices monitored by PSG in B1–B3 subgroups before and after treatment.

Group (cases)	OAI (times/h)		AHI (times/h)		$LSaO_2$ (%)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
B1 subgroup (68)	4.83 ± 2.99	1.50 ± 1.58	11.82 ± 16.21	7.24 ± 10.06	83.75 ± 3.15	91.58 ± 4.22
B2 subgroup (109)	5.32 ± 8.49	0.80 ± 0.90	16.30 ± 22.55	3.63 ± 2.02	83.65 ± 8.71	94.40 ± 2.04
B3 subgroup (119)	4.54 ± 5.52	0.38 ± 0.40	13.72 ± 15.11	1.97 ± 1.61	83.98 ± 7.72	94.26 ± 1.78
Between-group effect	$P < 0.05$		$P < 0.01$		$P < 0.001$	
Inter-group effect in B1 subgroup	$P < 0.001$		$P < 0.001$		$P < 0.001$	
Inter-group effect in B2 subgroup	$P < 0.001$		$P < 0.001$		$P < 0.001$	
Inter-group effect in B3 subgroup	$P < 0.001$		$P < 0.001$		$P < 0.001$	

Note: AHI, apnea hypopnea index; $LSaO_2$, the lowest recorded arterial oxygen saturation; OAI, obstructive apnea index; PSG, polysomnography.

in $LSaO_2$ (from 80.54 ± 7.60 to 90.14 ± 2.37, $P < 0.001$) and heart, lung, liver and kidney lesions (from 18 to 0, $P < 0.001$).

4. Discussion

The present study examined the efficacy of different treatment options for OSA in children. Using OSA-18 scores and PSG-derived measures as outcome indexes, we observed that in patients who did not undergo surgery (based on adenoid and tonsil size), the addition of NPSA to drug therapy improved treatment efficacy. Furthermore, in patients with more severe adenoid and tonsil grading, surgical intervention was superior to medical treatment, and longer periods of preoperative and postoperative drug therapy improved the results of surgery. Thus, results suggest that treatment of OSA should be individualized and tailored based on hypertrophy grade.

The management of OSA has three main aspects. The first is drug therapy, which alleviates adenoidal and tonsillar hypertrophy and inflammatory narrowing of the nasal cavity. Most children with OSA have varying degrees of rhinitis and sinusitis [4,17], implying that drug treatment should be implemented throughout the therapeutic program. The second is drainage of nasal secretions to alleviate congestion and airway narrowing. The third is surgery. Adenoidal/tonsillar hypertrophy is the main cause of OSA in children, hence surgical resection is the primary management option. Since the tonsils and adenoids in children have local immune functions and since adenotonsillectomy is not without risk of postoperative complications and recurrence, the decision to use surgery should be made carefully. To date, there are no international standardized recommendations for the indications and timing of surgery in children with OSA. For this reason, we included children with adenoid and tonsil sizes no higher than grade III into a non-surgical group.

Efficacy analysis in group A showed that although the OSA-18 scores in subgroup A1 improved, they did not reach normal levels, and indeed increased between 3 and 6 months after therapy. Similarly, despite improvements, OAI and AHI were not restored to 'normal' levels (<1 and <5, respectively). This indicates that drug therapy alone has a limited effect to alleviate upper airway obstruction, allowing for relapse after drug withdrawal. This is consistent with previous studies reporting benefits of drug therapy for mild OSA, but not full efficacy in all patients [31–35]. In contrast, the improvements in OSA-18 score, OAI and AHI in subgroup A2 were superior to those of subgroup A1, such that 3 months after treatment, these outcome measures reached 'normal' levels. Moreover, in subgroup A2, only a slight increase in OSA-18 occurred between 3 and 6 months post-therapy, and the value remained within the normal range. Taken together, our data suggest that adjuvant therapy with NPSA can improve the efficacy of drug treatment, presumably by removing upper airway secretions and facilitating drug access to the nasal cavity/nasopharynx.

Analysis of outcomes in group B revealed that OSA-18 scores in subgroup B1 (non-surgical) did not improve as rapidly or as much as those in surgical groups B2 and B3, with OSA-18 score, OAI and AHI not reaching values within the normal range. Additionally, the OSA-18 score showed an increase between 3 and 6 months post-treatment. This suggests that a non-surgical therapeutic program has only limited efficacy in treating grade IV adenoidal and tonsillar hypertrophy. Nonetheless, we suggest that this method can serve as a transitional therapy for children under 3 years of age, who have higher surgical risks.

Previous studies have documented improved quality of life scores and PSG findings after adenotonsillectomy in children with OSA, although symptoms can persist in patients with severe preoperative disease [10,11,36,37]. Although the OSA-18 score in subgroup B2 improved significantly during the first postoperative month, it subsequently progressively increased, perhaps due to inadequate treatment of rhinosinusitis by the short course of medication. Additionally in this subgroup, dyspnea and oxygen desaturation occurred in one child during induction of anesthesia, and in a further five children during postoperative extubation (all recovered after appropriate rescue). This may be related to inadequate preoperative therapy (only 3 days of medication) that did not satisfactorily correct the hypoxemia and improve vital organ function, resulting in poor tolerance of anesthesia and surgery. Subgroup B3, which had longer preoperative (2 weeks) and postoperative (3 months) drug therapy, showed no cases of anesthetic or surgical complications. In contrast to subgroups B1 and B2, OSA-18 score, OAI, AHI and $LSaO_2$ were restored to normal levels in subgroup B3, with the effect on OSA-18 score being fully maintained at 6 months. Hence, a longer preoperative regimen allowed for better toleration of anesthesia and surgery, despite an initially slower improvement in OSA-18. More extensive postoperative drug therapy appears to consolidate the efficacy to produce a sustained therapeutic effect. We suggest that conservative treatment is inadequate for children with a grade IV adenoid and/or tonsil. Surgical treatment had excellent efficacy after an adequate preoperative regimen that improves the condition of the patient. Furthermore, we recommend a full postoperative course of anti-inflammatory drug therapy to help prevent reoccurrence.

The present study is not without limitations. No control group was included, precluding determination of the magnitude of the efficacy of each therapy. Furthermore, because it was a retrospective study, patients were not randomized into the various groups, preventing direct comparisons of the treatment options, and potentially introducing bias. We grouped the patients according to size of tonsils and adenoids and the treatment strategies because we have previously found that size of adenoid/tonsil is positively

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correlated with the risk of OSA and the severity of the disease in children [38], but his may make interpretation of the results difficult. In addition, patient population was heterogeneous in terms of duration of disease and treatments. Asymptomatic patients with tonsillar hypertrophy could not be included because they were not diagnosed, resulting in a bias. Moreover, direct comparisons between therapeutic regimens could not be made for different levels of OSA severity. In addition, the follow-up period was limited to 6 months; longer-term studies are needed. Finally, since all grade III or <3 years-old patients were included in the non-surgical group, it is impossible to determine if these patients could benefit from surgery. Other countries may provide surgical treatment for patients <3 years-old, but we followed the Chinese guidelines, to provide drug therapy in combination with drainage of nasal secretions until the patient was older.

5. Conclusions

Management of OSA in children could be individualized and tailored according to patient age, adenoid and tonsil size, and disease severity. Conservative treatment (drug therapy plus NPSA) could be the primary choice for children with adenoids and tonsils grade ≤III, and surgical treatment for grade IV adenoids and tonsils, although drug therapy plus NPSA could be given in patients <3 years old as a transitional therapy to avoid surgical risks at this age. For children with moderate/severe OSA, adequate preoperative drug therapy with NPSA can lower the perioperative risk, and adequate postoperative drug therapy could improve surgical efficacy and reduce recurrence. Therefore, treatment choice should be based on the degree of hypertrophy, but it may not result in optimal outcomes. Prospective controlled studies are required to confirm these observations before they can be included in guidelines.

Conflict of interest statement

The authors declare no conflicts of interest.

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References

[1] M. Schlaud, M.S. Urschitz, P.M. Urschitz-Duprat, C.F. Poets, The German study on sleep-disordered breathing in primary school children: epidemiological approach, representativeness of study sample, and preliminary screening results, Paediatr. Perinat. Epidemiol. 18 (2004) 431–440.
[2] C.L. Marcus, Obstructive sleep apnea syndrome: differences between children and adults, Sleep 23 (Suppl. 4) (2000) S140–S141.
[3] S. Kotagal, Childhood obstructive sleep apnoea, BMJ 330 (2005) 978–979.
[4] C.L. Marcus, L.J. Brooks, K.A. Draper, D. Gozal, A.C. Halbower, J. Jones, et al., Diagnosis and management of childhood obstructive sleep apnea syndrome, Pediatrics 130 (2012) 576–584 (American Academy of Pediatrics).
[5] C. Flores-Mir, M. Korayem, G. Heo, M. Witmans, M.P. Major, P.W. Major, Craniofacial morphological characteristics in children with obstructive sleep apnea syndrome: a systematic review and meta-analysis, J. Am. Dent. Assoc. 144 (2013) 269–277.
[6] L.M. O'Brien, C.B. Mervis, C.R. Holbrook, J.L. Bruner, C.J. Klaus, J. Rutherford, et al., Neurobehavioral implications of habitual snoring in children, Pediatrics 114 (2004) 44–49.
[7] M.A. Nevin, Pediatric obesity, metabolic syndrome, and obstructive sleep apnea syndrome, Pediatr. Ann. 42 (2013) 205–210.
[8] D.A. Schwengel, N.M. Dalesio, T.L. Stierer, Pediatric obstructive sleep apnea, Anesthesiol. Clin. 32 (2014) 237–261.
[9] K.A. Waters, S. Suresh, G.M. Nixon, Sleep disorders in children, Med. J. Aust. 199 (2013) S31–S35.
[10] Y.S. Huang, C. Guilleminault, L.A. Lee, C.H. Lin, F.M. Hwang, Treatment outcomes of adenotonsillectomy for children with obstructive sleep apnea: a prospective longitudinal study, Sleep 37 (2014) 71–76.
[11] C.L. Marcus, R.H. Moore, C.L. Rosen, B. Giordani, S.L. Garetz, H.G. Taylor, et al.,Childhood Adenotonsillectomy Trial (CHAT), A randomized trial of adenotonsillectomy for childhood sleep apnea, N. Engl. J. Med. 368 (2013) 2366–2376.
[12] A.J. Lipton, D. Gozal, Treatment of obstructive sleep apnea in children: do we really know how? Sleep Med. Rev. 7 (2003) 61–80.
[13] S.E. Brietzke, D. Gallagher, The effectiveness of tonsillectomy and adenoidectomy in the treatment of pediatric obstructive sleep apnea/hypopnea syndrome: a meta-analysis, Otolaryngol.—Head Neck Surg. 134 (2006) 979–984.
[14] A. Ramirez, S. Khirani, S. Aloui, V. Delord, J.C. Borel, J.L. Pepin, et al., Continuous positive airway pressure and noninvasive ventilation adherence in children, Sleep Med. 14 (2013) 1290–1294.
[15] C.L. Marcus, G. Rosen, S.L. Ward, A.C. Halbower, L. Sterni, J. Lutz, et al., Adherence to and effectiveness of positive airway pressure therapy in children with obstructive sleep apnea, Pediatrics 117 (2006) e442–e451.
[16] B.C. Friedman, R.D. Goldman, Anti-inflammatory therapy for obstructive sleep apnea in children, Can. Fam. Physician 57 (2011) 891–893.
[17] E.O. Bixler, A.N. Vgontzas, H.M. Lin, D. Liao, S. Calhoun, A. Vela-Bueno, et al., Sleep disordered breathing in children in a general population sample: prevalence and risk factors, Sleep 32 (2009) 731–736.
[18] E. Dayyat, L. Kheirandish-Gozal, O. Sans Capdevila, M.M. Maarafeya, D. Gozal, Obstructive sleep apnea in children: relative contributions of body mass index and adenotonsillar hypertrophy, Chest 136 (2009) 137–144.
[19] M. Tagaya, S. Nakata, F. Yasuma, S. Miyazaki, F. Sasaki, M. Morinaga, et al., Relationship between adenoid size and severity of obstructive sleep apnea in preschool children, Int. J. Pediatr. Otorhinolaryngol. 76 (2012) 1827–1830.
[20] A. Ozkok, A. Kanbay, A.R. Odabas, A. Covic, M. Kanbay, Obstructive sleep apnea syndrome and chronic kidney disease: a new cardiorenal risk factor, Clin. Exp. Hypertens. 36 (2014) 211–216.
[21] X. Cheng, Y. Huang, Q. Zhao, E. Gu, Comparison of the effects of dexmedetomidine-ketamine and sevoflurane-sufentanil anesthesia in children with obstructive sleep apnea after uvulopalatopharyngoplasty: an observational study, J. Anaesthesiol. Clin. Pharmacol. 30 (2014) 31–35.
[22] J.M. Raurich, G. Rialp, J. Ibanez, C. Campillo, I. Ayestaran, C. Blanco, Hypercapnia test as a predictor of success in spontaneous breathing trials and extubation, Respir. Care 53 (2008) 1012–1018.
[23] C.L. Marcus, J.L. Carroll, O. Bamford, P. Pyzik, G.M. Loughlin, Supplemental oxygen during sleep in children with sleep-disordered breathing, Am. J. Respir. Crit. Care Med. 152 (1995) 1297–1301.
[24] R.A. Franco Jr., R.M. Rosenfeld, M. Rao, First place—resident clinical science award 1999. Quality of life for children with obstructive sleep apnea, Otolaryngol. Head Neck Surg. 123 (2000) 9–16.
[25] A.M. Strocker, A. Carrer, N.L. Shapiro, The validity of the OSA-18 among three groups of pediatric patients, Int. J. Pediatr. Otorhinolaryngol. 69 (2005) 241–247.
[26] Editorial Board of Chinese Journal of Otorhinolaryngology Head-and Neck Surgery: Chinese Otorhinolaryngology of Chinese Medical Association, Draft of guidelines for the diagnosis and treatment of pediatric sleep apnea hypopnea syndrome, (Urumqi), Zhonghua Er Bi Yan Hou Tou Jing Wai Ke Za Zhi 42 (2007) 83–84.
[27] M. Friedman, H. Tanyeri, M. La Rosa, R. Landsberg, K. Vaidyanathan, S. Pieri, et al., Clinical predictors of obstructive sleep apnea, Laryngoscope 109 (1999) 1901–1907.
[28] R.E. Gliklich, R. Metson, Techniques for outcomes research in chronic sinusitis, Laryngoscope 105 (1995) 387–390.
[29] Y.Q. Tian, A.H. Sun, Otolaryngology Head & Neck Surgery, People's Medical Publishing House, Beijing, 2007.
[30] V.J. Lund, H. Stammberger, W.J. Fokkens, T. Beale, M. Bernal-Sprekelsen, P. Eloy, et al., European position paper on the anatomical terminology of the internal nose and paranasal sinuses, Rhinol. Suppl. 24 (2014) 1–34.
[31] L. Kheirandish-Gozal, D. Gozal, Intranasal budesonide treatment for children with mild obstructive sleep apnea syndrome, Pediatrics 122 (2008) e149–e155.
[32] Y.G. Jung, H.Y. Kim, J.Y. Min, H.J. Dhong, S.K. Chung, Role of intranasal topical steroid in pediatric sleep disordered breathing and influence of allergy, sinusitis, and obesity on treatment outcome, Clin. Exp. Otorhinolaryngol. 4 (2011) 27–32.
[33] M. Berlucchi, L. Valetti, G. Parrinello, P. Nicolai, Long-term follow-up of children undergoing topical intranasal steroid therapy for adenoidal hypertrophy, Int. J. Pediatr. Otorhinolaryngol. 72 (2008) 1171–1175.
[34] A.D. Goldbart, S. Greenberg-Dotan, A. Tal, Montelukast for children with obstructive sleep apnea: a double-blind, placebo-controlled study, Pediatrics 130 (2012) e575–e580.
[35] L. Zhang, R.A. Mendoza-Sassi, J.A. Cesar, N.K. Chadha, Intranasal corticosteroids for nasal airway obstruction in children with moderate to severe adenoidal hypertrophy, Cochrane Database Syst. Rev. 3 (2008) CD006286.
[36] M.G. Stewart, D.G. Glaze, E.M. Friedman, E.O. Smith, M. Bautista, Quality of life and sleep study findings after adenotonsillectomy in children with obstructive sleep apnea, Arch. Otolaryngol. Head Neck Surg. 131 (2005) 308–314.
[37] R.B. Mitchell, Adenotonsillectomy for obstructive sleep apnea in children: outcome evaluated by pre- and postoperative polysomnography, Laryngoscope 117 (2007) 1844–1854.
[38] L. Shen, Z. Lin, Y. Xu, Z. Yang, The relationship between obstructive sleep apnea hypopnea syndrome and adenoid size as well as tonsil size in children, Lin Chung Er Bi Yan Hou Tou Jing Wai Ke Za Zhi 28 (2014) 381–385.

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